# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**65-059**

# APPROVAL LETTER

ANDA 65-059

NOV 24 2000

Ranbaxy Pharmaceuticals, Inc.
Attention: Shirley Ternyik
U.S. Agent for Ranbaxy Laboratories Limited
600 College Road East
Princeton, NJ 08540

Dear Madam:

This is in reference to your abbreviated new drug application dated December 17, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Amoxicillin Tablets USP, 500 mg and 875 mg. We note that this product is subject to the exception provisions of Section 125(d)(2) of Title I of the Food and Drug Administration Modernization Act of 1997.

Reference is also made to your amendment dated August 8, 2000.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Amoxicillin Tablets USP, 500 mg and 875 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Amoxil® Tablets, 500 mg and 875 mg, respectively, of SmithKline Beecham Pharmaceuticals). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

Gary Buehler

Gary Buehler 11/24/00
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

**ANDA APPROVAL SUMMARY**

**AADA:** 65-059

**DRUG PRODUCT:** Amoxicillin Tablets, USP

**FIRM:** Ranbaxy Laboratories Ltd.

**DOSAGE FORM:** Tablets **STRENGTH:** 500 mg and 875 mg

**CGMP STATEMENT/EIR UPDATE STATUS:** A signed cGMP certification was provided on pages 1196, Vol. 1.7. Acceptable EER for the finished dosage manufacturer is dated 3/13/00. Inspection of the drug substance supplier is pending.

**BIO STUDY:** The bio-study conducted on the applicant's product and Amoxil Tablets manufactured by SmithKline Beecham Pharmaceuticals was found acceptable by the Division of Bioequivalence on 3/29/00. The waiver for bio-study for the 500 mg tablet was found acceptable on 12/23/99.

**METHOD VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):** The drug substance and drug product are both USP. The applicant is using USP methods in testing the bulk drug and finished product. An exception is the assay for related substances which is based on the monograph for Amoxicillin found in the European Pharmacopoeia.

**STABILITY - (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?):** Accelerated and room temperature stability data support the proposed 24 month expiration date. Containers used in the stability studies were identical to those described in the container section. The exception is the stability study of the bulk storage package, which uses a simulated package design.

**LABELING:** Refer to the Division of Labeling "Approval Summary" dated 8/23/00.

**STERILIZATION VALIDATION (IF APPLICABLE):** Not-applicable to this drug product.

**SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?):** Exhibit batch AMT***02LF (500 mg) and AMTX**02LF (875 mg) were used for stability and bio-studies. Both batches were manufactured with

bulk drug substance from Ranbaxy Laboratories Ltd., Toansa, Punjab, India. Batch AMT***02LF (500 mg) consisted of tablets (theoretical ‹**02LF (875 mg) consisted ablets (theoretical

**SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?):** See above

**PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?):** The proposed production batch size for 500 mg strength is tablets and for 875 mg strength is tablets. The manufacturing process described in the master production record is the same as that described in the exhibit batch record.

**CHEMIST:** Susan Zuk **DATE:** 8/17/00
**SUPERVISOR:** Richard Adams **DATE:** 8/25/00

R.C. Adams

65-059

Pharmaceuticals Inc.
Agent for: Ranbaxy Laboratories Limited
Attention: Shirley Ternyik
College Road East
Princeton, NJ 08540

FEB - 8 2000

Madam:

Please refer to your abbreviated new drug application (ANDA) dated December 22, 1999, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Amoxicillin Tablets USP, 400 mg and 875 mg.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical chemical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(2) for the following reasons:

The bioequivalence study submitted to support the approval of your application has been determined to be incomplete. You have failed to provide a post-prandial, single dose *in vivo* bioequivalence study for your proposed product. If you have questions regarding your bioequivalence study, or bioequivalence requirements for this product, please contact Lizzie Sanchez, Pharm.D., Project Manager, Division of Bioequivalence, at (301) 827-5847 for further guidance.

The concentration of the inactive ingredient, [redacted] in your proposed drug product exceeds the maximum concentration of this inactive ingredient previously approved by the Agency in an oral drug product. Please provide examples of approved drug products administered by the same route of administration which contain this inactive ingredient in the same concentration range, a quantitative breakdown of the ingredient, a DMF authorization letter from the manufacturer, or provide information demonstrating that this inactive ingredient in this concentration does not affect the safety of the proposed drug product.

Please provide a list of addresses of the suppliers of your inactive ingredients.

Please provide a letter of authorization from the DMF holder, , for the screw cap/closure system.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3). If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Emily Thomas
Project Manager
(301) 827-5862

Sincerely yours,

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research